PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Artcle 36 and Rule 70)

Applicant's or agent's file reference PCA31166/HMY	**FOR FURTHER ACTION**	SeeNotificationofTransmittalofInternationalPreliminary Examination Report (Form PCT/IPEA/416)
International application No. **PCT/KR2003/002388**	International filing date *(day/month/year)* **07 NOVEMBER 2003 (07.11.2003)**	Priority date *(day/month/year)* 08 NOVEMBER 2002 (08.11.2002)

International Patent Classification (IPC) or national classification and IPC

IPC7 A61K 9/107

Applicant

HANMI PHARM. CO., LTD. et al

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 3 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of _____ sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demamd	Date of completion of this report
07 JUNE 2004 (07.06.2004)	27 DECEMBER 2004 (27.12.2004)
Name and mailing address of the IPEA/KR Korean Intellectual Property Office 920 Dunsan-dong, Seo-gu, Daejeon 302-701, Republic of Korea Facsimile No. 82-42-472-7140	Authorized officer Yoon, Kyung Ae Telephone No. 82-42-481-5605

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International aplication No.
PCT/KR2003/002388

I. Basis of the report

1. With regard to the elements of the international application:*

[X] the international application as originally filed

[ ] the description:
pages _____ , as originally filed
pages _____ , filed with the demand
pages _____, filed with the letter of _____

[ ] the claims:
pages _____ , as originally filed
pages _____ , as amended (together with any statment) under Article 19
pages _____ , filed with the demand
pages _____, filed with the letter of _____

[ ] the drawings:
pages _____ , as originally filed
pages _____ , filed with the demand
pages _____, filed with the letter of _____

[ ] the sequence listing part of the description:
pages _____ , as originally filed
pages _____ , filed with the demand
pages _____, filed with the letter of _____

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language English which is

[ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

[X] the language of publication of the international application(under Rule 48.3(b)).

[ ] the language of the translation furnished for the purposes of international preliminary examination(under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide** and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

[ ] contained inthe international application in written form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readable form

[ ] The statement that the subsequently furnished written sequence listing does not go beyond the disc losure in the international applicationas as filed has been furinshed.

[ ] The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. [ ] The amendments have resulted in the cancellation of:

[ ] the description, pages _____

[ ] the claims, Nos. _____

[ ] the drawings, sheets _____

5. [ ] This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box(Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed." and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item I and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION

International aplication No.
PCT/KR2003/002388

V. **Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	1-11	YES
	Claims	none	NO
Inventive step (IS)	Claims	1-11	YES
	Claims	none	NO
Industrial applicability (IA)	Claims	1-11	YES
	Claims	none	NO

2. Citations and explanations (Rule 70.7)

The present invention relates a microemulsion concentrate comprising a water-insoluble anti-cold drug, a surfactant and an oil, which is prepared by a method comprising (a) dissolving the water-insoluble anti-cold drug in a co-surfactant to obtain a homogeneous drug solution; (b) adding the surfactant and the oil in the drug solution to obtain a microemulsion pre-concentrate; and (c) removing the co-surfactant from the preconcentrate.

The following documents have been considered for the purpose of this report:
D1 = US 4388307 A (14. 06. 1983)
D2 = US 6190646 B1 (20. 02. 2001)
D3 = WO 99-39700 A1 (12. 08. 1999)

1. Novelty and Inventive Step
D1 discloses a liquid pharmaceutical composition comprising a cyclosporin, a trans-esterification product of a hydrogenated vegetable oil triglyceride and a polyalkylene polyol, a vegetable oil and ethanol.
D2 discloses a microemulsion comprising a nitrogenous compounds, an alkyl phosphoric ester surfactant, a cosurfactant, a vegetable oil and a plasticizer.
D3 discloses a pharmaceutical composition in the form of solid nanoparticles, which comprises a mixture of a lipidic material and an amphiphilic material, a surfactant, a cosurfactant and a pharmaceutically active substances.

However, none of the documents D1-D3 disclose a microemulsion preconcentrate a water-insoluble anti-cold drug which is prepared by removing the co-surfactant (ethanol) from the preconcentrate. Moreover, the applicants have supplied data showing that the microemulsion concentrates according to the present invention exhibit higher dissolution rates and improved bioavailability of the drug compared to the comparative preparation (Figure 1 and 3). Accordingly, the present invention is not considered to be easily invented from the inventions disclosed in D1-D3 by a person skilled in the art. Therefore, the novelty and inventive step of the present invention can be acknowledged, and claims 1 to 11 meet the requirements of PCT Article 33(2) and 33(3).

2. Industrial Applicability
Claims 1 to 11 appear to meet the requirement of PCT Article 33(4).